UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/281,760	03/30/1999	ROBERT LAWTON	241/08	7613

27239 7590 05/07/2002

IDEXX
C/O HOWREY SIMON ARNOLD & WHILE LLP - SD
301 RAVENSWOOD AVENUE
MENLO PARK, CA 94025

EXAMINER	
JAMROZ, MARGARET E	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/07/2002 29

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/281,760	LAWTON ET AL.	
	Examiner	Art Unit	
	Margaret E Jamroz	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-115* is/are pending in the application.

4a) Of the above claim(s) *3-5,12-14,18-20,24-26,31-33,38-40, and 44-115* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-11,15-17,21-23,27-30,34-37 and 41-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The examiner of your application in the PTO have changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Megan Jamroz, Art Unit 1644, Technology Center 1600.

2. Applicant's amendment, filed 11/19/01 (Paper No. 24), is acknowledged.

Claims 1-115 are pending.

Claims 3-5, 12-14, 18-20, 24-26, 31-33, 38-40, and 44-115 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to non-elected inventions. Claim 5 is withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to non-elected species.

Claims 1-2, 6-11, 15-17, 21-23, 27-30, 34-37, and 41-43 are under consideration in the instant application.

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/12/2002 has been entered.

4. The examiner notes that on page 4, paragraph 4 of the amendment filed 11/28/2001, it appears that applicant intended to cancel claims 9-11, 17, 23, 28, 30, 35, and 37. However, the amendment to the claims beginning on page 2 of the same amendment does not state that claims 9-11, 17, 23, 28, 30, 35, and 37 should be canceled; therefore, said claims are pending until such time that applicant formally cancels said claims.

Claim objections

5. Claims 9 and 11 are objected to because they are dependent claims and the sentences should start with "The".

6. Claim 28 is objected to because of the following informalities: in line 3, "consists of from 5 to 71 amino acids" should be amended to "consists of 5 to 71 amino acids". Appropriate correction is required.

7, Claim 11 is objected to because of the following informalities: in line 4, "consists of from 5 to 71 amino acids" should be amended to "consists of 5 to 71 amino acids". Appropriate correction is required.

8 Claim 35 is objected to because of the following informalities: in line 3, "consists of from 5 to 71 amino acids" should be amended to "consists of 5 to 71 amino acids". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112.

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 17, 23, 30, 37, and 41are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments filed 11/28/2001 have been fully considered but they are not persuasive.

(a) In claims 17, 23, 30, and 37, the recitation of the term "recombinant specific binding molecule" renders the claims ambiguous and indefinite. Said term has no specific well-known meaning within the art and has not been defined in the specification. Further, the claims upon which claims 17, 23, 30, 37, depend are

drawn to "specific binding proteins" which are not recombinant and do not encompass the genus of "molecules". Applicant's position is that the rejection is moot as the claims have been canceled. It is the examiner's opinion that until the claims are officially canceled, the rejection remains.

(b) In claim 41, the recitation of the laboratory designation "8H.8" renders the claims ambiguous and indefinite. Applicant's position is that one skilled in the art would understand what is claimed in light of the specification. The examiner's opinion remains that different laboratories often use the same name to describe completely different proteins, therefore, the claim is indefinite. Applicant can overcome this rejection by reciting the ATCC designation for the hybridoma and the antibody it produces.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 41-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons set forth in Paper Nos. 16 and 22, mailed 5/21/2001 and 10/24/2000, respectively, and the reasons set forth below.

Applicant's position is that the Office has only made a bald assertion that the claims are not enabled in the action mailed 5/21/2001 (Paper No. 22) and has not provided sound reasoning to support such questioning the enablement of making the monoclonal antibody 8H.8. Further, applicant refers the examiner to citations on page 4, line 27 through page 5, line 6 which states that literature citations and co-pending applications disclose the canine IgE amino acid sequence.

(A) With respect to the biological deposit issues, the examiner refers applicant to the requirements for Biological deposits as set forth in MPEP 2400 and 37 CFR 1.801-1.809.

For further clarification of the previous rejections, the following is noted by the examiner. It is the examiner's opinion that the rejection set forth in Paper No. 22, mailed 5/21/2001 was maintained for the reasons of record set forth in Paper No. 16, mailed 10/24/2000, which did not need to be reiterated.

The monoclonal antibody 8H.8 recited in claim 41 is essential to the claimed invention. The reproduction of monoclonal antibody 8H.8 from the C-terminal 71 amino acids of exon 3 of canine IgE is an extremely unpredictable event. The monoclonal antibody 8H.8 disclosed on page 24, paragraph 2 of the specification, must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The instant specification does not disclose a repeatable process to obtain the monoclonal antibody 8H.8, and it is not apparent if the monoclonal antibody 8H.8 is readily available to the public.

If the deposits have been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the monoclonal antibody 8H.8 have been deposited under the Budapest Treaty and that the monoclonal antibody 8H.8 will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit, 5 years after the last request for a sample, or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806.

If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Amendment of the specification to disclose the date of deposit and the complete name and address of the depository is required.

If the deposit was made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the monoclonal antibody 8H.8 described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 CFR 1.801-1.809 for further information concerning deposit practice.

(B) Further, with respect to the citations on page 4, lines 27 to page 5, line 6, applicant sets forth the teachings of Patel et al. (Immunogenetics 4: 282-286, 1995) and co-pending applications 08/800,698, filed 2/14/1997, 09/146,400, filed 9/3/1998, and 09/146,617, filed 9/3/1998 which disclose the amino acid sequence of canine IgE.

In the absence of a specific SEQ ID NO disclosing an amino acid sequence of canine IgE, it is impossible to determine what the C-terminal 71 amino acids of canine IgE are for immunizing mice to make the monoclonal antibody 8H.8; therefore, applicant has not taught how to make the claimed invention.

The incorporation of essential material in the specification by reference to a foreign application or patent, a non-allowed U.S. patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112; however this does not bar incorporation by reference. Ex parte Schwarze, 151 USPQ 426 (Bd. of Appeals, 1966). "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112).

The attempt to incorporate subject matter into this application by reference to Patel et al. (Immunogenetics 4: 282-286, 1995) and co-pending applications 08/800,698, filed 2/14/1997, 09/146,400, filed 9/3/1998, and 09/146,617, filed 9/3/1998 is improper because an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, subject to the conditions forth in the MPEP 608.01(p).

The canine IgE sequence taught by Patel et al. (Immunogenetics 4: 282-286, 1995) and co-pending applications 08/800,698, filed 2/14/1997, 09/146,400, filed 9/3/1998, and 09/146,617, filed 9/3/1998 is essential for prosecution of the instant application because the positions of the C-terminal 71 amino acids of canine IgE cannot be determined in the absence of the sequence of the canine IgE. Applicant should submit the amino acid sequence taught by Patel et al. (Immunogenetics 4: 282-286, 1995) as a SEQ ID NO and amend the specification, brief description of the drawings, and Figures in accordance with the sequence compliance rules indicated above.

Until such time that the requirements set forth for biological deposits and proper incorporation of the canine IgE amino acid sequence are met in-full, it is the examiner's opinion that the claims shall remain not enabled. Applicant is required to deposit the claimed monoclonal antibody 8H.8.

11. Claims 1-2, 6-11, 15-17, 21-23, 27-30, and 34-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a specific binding protein which specifically binds to native canine free or B cell-bound IgE, and does not bind to IgE when the IgE is bound to a FcεRI receptor on a mast cell, including an IgE expressed on the surface of a canine B cell and a specific binding protein which comprises an antibody which binds to the peptides consisting of SEQ ID NOS: 4-5 and conservative variants thereof, does not reasonably provide enablement for for the composition or method above further comprising a specific binding protein which does not bind to IgE when the IgE is bound to any receptor other than FcεRI on a mast cell (claim 1); an antibody ... raised to ... a peptide ... wherein said peptide consists of from 5 to 71 amino acids (claims 11, 28, and 35); a specific binding protein which specifically binds the genus of peptides comprising a leucine positioned two peptide binds away from a tyrosine-arginine pair (claims 7 and 11); a specific binding protein which specifically binds a peptide comprising SEQ ID NOS 1-5 (claims 6-7, 15, 21, 27, and 34); a specific binding protein which specifically binds a peptide consisting of SEQ ID NOS 1-3 (claim 7); or an antibody which can bind any variant caused by a non-conservative mutation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the reasons set forth in Paper Nos. 22 and 16, mailed 5/21/2001 and 10/24/2000, respectively, and the reasons set forth below.

Applicant's position is that the claims have been amended to recite a specific binding protein selected from the group consisting of a monoclonal or polyclonal antibody and fragments thereof, a hybrid antibody, and a single chain antibody which are well-known in the art and are enabled.

It is the examiner's opinion that the specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Claim 1 recites in lines 5-6 "the IgE bound to a receptor on a mast cell". There is insufficient guidance and support in the specification to support IgE bound to any receptor other than to FcεRI on the surface of a mast cell.

The specification on pages 14-15 defines conservative variants as those amino acid residues that are mutated such that the amino acid residue encoded by the codon is not altered. The specification does not provide sufficient support for the genus of variants which encompasses mutations that do result in changes of the amino acid residue.

Due to ambiguity of the antibody of claim 41, one skilled in the art would not which amino acid sequences are recognized by the antibody. Further, claim 43 recites a specific binding protein ... which specifically binds to the defined epitope bound by the antibody of claim 41. Claims 41-42 do not defined the epitope to which the antibody is supposed to bind. The genus encompasses antibodies that can bind epitopes wherein such epitopes have unlimited differences in amino acid sequences, including numerous differences in linear and conformational epitopes.

However, the present specification fails to provide sufficient disclosure of such broadly recited epitopes that maintain the structural and functional properties of the epitopes set forth in SEQ ID NOS: 4-5 (i.e. canine IgE epitopes. The specification does not provide sufficient guidance as to which of the amino acids may be changed while "epitope" structural or functional activity and specificity is retained.

The specification discloses only that the claimed binding protein (an antibody): binds soluble and ELISA solid phase native IgE, peptides consisting of SEQ ID NOS: 4 and 5, and presumably the 71 amino acid peptide which was used in the immunizations that produced the antibody. Claims 6-11, 15-17, 21-23, 27-30, 34-37 recite specific binding proteins that bind to peptides "comprising" SEQ ID NOS: 1-5.

"Comprising" is open term language and includes amino acids outside of the disclosed sequences, however, applicant has not provided any guidance as to what those amino acid sequences are, and if the antibody is capable of binding to the broadly encompasses undefined sequences. There is insufficient guidance and direction as to make and use canine IgE peptide specific antibodies wherein the antibodies and antigen binding fragments thereof bind a peptide "comprising" SEQ ID NOS: 1-5, the genus of undefined epitopes, or the genus of epitopes from 5-71 amino acids in length.

The genus encompasses antibodies that can specifically bind canine IgE peptides wherein such peptides have numerous differences in amino acid sequences at positions other than the defined peptides consisting of SEQ ID NOS: 1-5, including numerous differences in linear and conformational epitopes.

One skilled in the art could not begin to comprehend the unlimited combinations of amino acids to make up a "defined epitope" as recited in claims 29-30, 36-37, and 42-43, as applicant has not defined the structure of the genus of "epitopes". Further, claims 11, 28, and 35 recite a specific binding protein which is raised against a peptide wherein the peptide from which the specific binding protein is raised to consists of from 5-71 amino acids. Claims 11, 28, and 35 depend on claims 6, 27, and 34, respectively wherein the peptides are fragments of 5-11 amino acids as recited in SEQ ID NOS: 4-5. The specification does not provide any guidance as to what the other amino acid sequences "comprising" such amino acid sequences are.

However, the present specification fails to provide sufficient disclosure of such canine IgE peptides that maintain the structural and functional properties of the peptides set forth in SEQ ID NOS: 4-5 wherein 5-11 amino acids are defined and the other amino acids can vary. The specification does not provide sufficient guidance as to which of the amino acids may be added or changed while canine IgE peptide structural or functional activity and specificity is retained.

Coleman et al. (Research in Immunology, 1994; 145(1): 33-36) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza et al., of record, (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444) teaches single amino acid substitutions outside the antigenic site on a protein effect antibody binding. Futher, Lederman et al., of record, (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

The scope of the claimed peptide-specific antibodies is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of epitopes broadly encompassed by the claimed invention. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's or peptide's amino acid sequence, and still retain similar biological activity or structural specificity requires a knowledge of and guidance with regard to

which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a limited number of proteins/nucleic acids and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Because of this lack of guidance, the extended experimentation that would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al.; in The Protein Folding Problem and Tertiary Structure Prediction,1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), it would require an undue amount of experimentation for one of skill in the art to arrive at the other peptides encompassed by the claimed invention.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

12. Claims 1-2, 6-11, 15-17, 21-23, 27-30, and 34-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in Paper Nos. 22 and 16, mailed 5/21/2001 and 10/24/2000, respectively, and the reasons set forth below.

Applicant's position is that the claims have been amended to comply with the written description guidelines.

It is the examiner's opinion that applicant is in possession of antibodies which bind to canine IgE peptides consisting of SEQ ID NOS: 4-5 which; however, applicant is not in possession of any antibody against any the genus of peptides "comprising" SEQ ID NOS: 1-5 or consisting of SEQ ID NOS: 1-3, or any the genus of undefined peptides consisting of, or comprising, any other undefined sequence. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of polypeptide sequences may be achieved by means of a recitation of a representative number of antibodies which specifically bind peptides "comprising" SEQ ID NOS: 4-5, or any the genus of undefined peptides consisting of, or comprising, any other sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The following are new grounds of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-2, 6-11, 15-16, 21-22, 27-29, and 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,514,776 in view of U.S. Patent 5,629,415.

The '776 patent teaches monoclonal and polyclonal antibodies raised against chemically synthesized canine IgE peptides of 41-72 amino acids in length (i.e. isolated and purified peptides within the range of 5-71 amino acids) and coupled to KLH prior to immunization of mice (see the columns 5, section 7 and column 6 in particular). The antigenic epitopes of the invention (i.e. peptides representing the epitopes) are present on dog B cell membrane-bound immunoglobulins, but not on the secreted soluble form of the immunoglobulin, and are useful for therapeutic purposes (i.e. treatment of canine allergies; see column 2, paragraph 3 in particular). The '776 patent further teaches monoclonal and polyclonal antibodies against dog IgE (see column 5, lines 19-21 in particular). The monoclonal antibodies of the '776 patent do not induce histamine release from basophils and mast cells, and specifically targets IgE-bearing B cells for the

treatment of canine hypersensitivity (see column 1, lines 55-67 through column 2 paragraph 1 in particular). The peptides were more effective as immunogens in the production of antibodies when conjugated to a protein carrier. Further, "multiple molecules of peptides can be conjugated to each molecule of the carrier protein. With KLH, a preferred molar ratio for peptide/KLH is 10" (see column 6, paragraphs 4 and 5 in particular). The specifically defined epitopes are toward the N-terminus and contain 13-27 amino acid residues and are highly acidic and hydrophilic. They are located on the extracellular surface of the plasma membrane, and are exposed and accessible to antibodies (see column 2, paragraphs 5-6 in particular). "If an antigenic epitope of IgE is present on B cells and not on basophils and mast cells, these epitopes ... are virtually unique cell surface markers of IgE-bearing B cells and antibodies against them do not produce histamine release. These markers, therefore, provide targets for several types of monoclonal or polyclonal antibody-based therapy for IgE-mediated allergic diseases, and provide a means to differentiate B cells producing IgE from B cells producing other isotypes" (see column 2, lines 62-67 through column 3, lines 1-4 in particular).

The'776 patent does not teach monoclonal or polyclonal antibodies which recognize SEQ ID NOS: 1 or 3-5 which contain the L-Xaa-Xaa-Y-R motif.

The '415 patent teaches a specific binding protein (i.e. monoclonal and polyclonal antibodies) which can bind to full-length canine IgE or peptide fragments of canine IgE (see column 2, paragraph 1; column 7, paragraph 5; and column 8, paragraph 4 in particular). The antibodies are raised against epitopes present in B cell associated IgE (i.e. membrane bound), and that "inhibition of binding of IgE to its receptor on mast cells may be a way to control allergic responses" (see column 1, paragraph 5; and column 2, paragraph 1 in particular). SEQ ID NO: 2 of the '425 patent is the amino acid sequence of canine IgE, residues 245-255 of SEQ ID NO: 2 are identical to SEQ ID NO: 5, and said residues include the L-Xaa-Xaa-Y-R motif. Further, "comprising" is open language and includes amino acid residues outside of the claimed peptide fragments. Claims 34 and 36 are included because even though the reference antibody was not raised to a recombinant plant virus particle comprising at least one copy of an isolated and purified peptide comprising SEQ ID NOS: 4 or 5, the antibodies would bind to the L-Xaa-Xaa-Y-R motif regardless of how it is produced.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the substitute the specific isolated and purified canine IgE peptides taught by the '415 patent to make the specific binding proteins taught by the '776 patent which specifically bind to a native canine B cell-bound IgE, and which does not bind to IgE when the IgE is bound to a receptor on a mast cell. Although the '415 patent is silent about the antibodies binding to SEQ ID NOS: 1 and 3-5, the antibodies inherently would bind to these sequences. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind to SEQ ID NOS: 1 and 3-5 recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980). Claim 8 is included because even if one amino acid is changed, there are sufficient remaining non-mutated residues to which the antibody can bind.

One of ordinary skill in the art would have been motivated to make a specific binding protein comprising polyclonal or monoclonal antibodies which specifically binds to a native canine B cell-bound IgE or to peptides consisting of canine IgE sequences because the '415 patent teaches that "inhibition of binding of IgE to its receptor on mast cells may be a way to control allergic responses", and the polyclonal and monoclonal antibodies do not induce histamine release from basophils and mast cells, and specifically targets IgE-bearing B cells for the treatment of canine hypersensitivity as taught by the '776 patent.

14. Claims 17, 23, 30, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,514,776 in view of U.S. Patent 5,629,415 as applied to claims 1-2, 6-7, 9-11, 15-16, 21-22, 34-36 above, and further in view of U.S. Patent 5,670,626

The '776 and '415 patents have been discussed supra.

The combined reference teachings do not teach a recombinant binding protein.

The '626 patent teaches that it is possible to identify human monoclonal antibodies with antigen specificity of interest. The more recent development of methodologies to construct recombinant phage incorporating human V_H and V_L libraries have added another powerful tool in the identification of antibody species of interest. Additionally, the recombinant technology has "enabled to production of human monoclonal antibodies in large quantities" (see column 2, paragraph 2 in particular). The antibodies of the invention are used to treat allergic diseases (see the entire document).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the substitute the specific isolated and purified canine IgE peptides taught by the '415 patent to make the specific binding proteins taught by the '776 patent which specifically bind to a native canine B cell-bound IgE, and which does not bind to IgE when the IgE is bound to a receptor on a mast cell.

One of ordinary skill in the art would have been motivated to make a recombinant specific binding protein comprising polyclonal or monoclonal antibodies which specifically bind to a native canine B cell-bound IgE or to peptides consisting of canine IgE sequences because the '415 patent teaches that "inhibition of binding of IgE to its receptor on mast cells may be a way to control allergic responses"; the polyclonal and monoclonal antibodies do not induce histamine release from basophils and mast cells, and specifically targets IgE-bearing B cells for the treatment of canine hypersensitivity as taught by the '776 patent; and the recombinant technology has "enabled to production of human monoclonal antibodies in large quantities" as taught by the '626 patent.

The following is a new ground of rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112.

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 11, 16-17, 22-23, 29-30, 36-37, and 42-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 11 recites the limitation "An antibody of claim 9" in line 1. There is insufficient antecedent basis for this limitation in base claim 9. Base claim 9 is drawn to a specific binding protein.

(b) Claims 16-17, 22-23, 29-30, 36-37, and 42-43 are indefinite and ambiguous in the recitation of a "defined epitope" The specification has not defined the genus of amino acid sequences which are encompassed by "defined epitope" which are relevant to the claimed invention.

16. No claim is allowed.

17. The drawings are objected to because of the errors listed on the PTO-948; therefore, the drawings fail to comply with 37 CFR 1.84.

The Patent and Trademark Office no longer makes drawing changes. See 1017 O.G. 4. It is applicant's responsibility to ensure that the drawings are corrected. Corrections must be made in accordance with the instructions below.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Megan Jamroz, whose telephone number is (703) 308-8365. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Margaret (Megan) Jamroz, Ph.D.
Patent Examiner
Technology Center 1600
April 24, 2002

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600